mg/m2 (IRMA 1, 2, 3, 5) or Cetuximab 400 mg/m2 (IRMA 4). A dose of 67.5 Gy in 30 fractions (IRMA 1, 2, and 4) or 70.5 Gy in 30 fractions (IRMA 3, 4, and 5) was delivered to primary tumor and involved nodes, 60 Gy were delivered to high risk and 55.5 Gy to low risk lymph node areas. Static (IMRT) or volumetric (VMAT) intensity modulated technique with simultaneous integrated boost was used.

Results: 107 patients (median age 56 years, range 30-78, UICC stage III: n = 18, IV: n = 89) were included in this analysis. IC was performed with Cisplatin + 5-Fluorouracil in 65 (61%) patients and with Docetaxel + Cisplatin + 5-Fluorouracil in 42 (39%) cases. Concomitant Cisplatin and Cetuximab were administered in 84% and in 16% of patients, respectively. 51% (n = 55) of cases were irradiated with step & shoot IMRT-SIB technique (7 beams), while 49% (n = 52) of patients were irradiated with VMAT-SIB (two arcs) technique. During radio-chemotherapy, 23 (21%) patients developed mucositis, 12 (11%) G3 dysphagia and 10 (9.3%) G3 hematological toxicity. Even 1 (0.9%) G4 leukopenia and 3 (2.8%) G5 (2 neutropenia and one fatal myocardial infarction) adverse events were observed. The overall response rate after radio-chemotherapy was 82.2%. Two-year local control and survival were 64.2% and 64.6% (IRMA 1), respectively, 57.8% and 56.2% (IRMA 2), 66.4% and 75.5% (IRMA 3), 70.1% and 66.7% (IRMA 4), and 76.5% and 82.4% (IRMA 5), respectively.

Table IRMA and studies related toxicity

IRMA* 1	IRMA* 2	IRMA* 3	IRMA* 4	IRMA* 5
3 CF → C+IMRT/VMAT (67,5-60-55,5 Gy/30 fx)	3 DCF → C+IMRT/VMAT (67,5-60-55,5 Gy/30 fx)	3 DCF → C+IMRT/VMAT (70,5-60-55,5 Gy/30 fx)	3 CF → Cetuximab+IMRT/VMAT (67,5/70,5 -60-55,5 Gy/30 fx)	3 CF → C+IMRT/VMAT (70,5-60-55,5 Gy/30 fx)
n° pts = 28	n° pts = 16	n° pts = 26	n° pts = 17	n° pts = 20
Mucositis: G3: 29% G4: 0% Disfagia: G3: 11% G4: 0% Haematological toxicity G3: 25% G4: 0% G5: 3% Myocardial infarction G5: 3%	Mucositis: G3: 19% G4: 0% Disfagia: G3: 12% G4: 0% Haematological toxicity G3: 37% G4: 12% G5: 0%	Mucositis: G3: 15% G4: 0% Disfagia: G3: 7% G4: 0% Haematological toxicity G3: 4% G4: 0% G5: 4%	Mucositis: G3: 29% G4: 0% Disfagia: G3: 18% G4: 0% Haematological toxicity G3: 6% G4: 6% G5: 0%	Mucositis: G3: 15% G4. 0% Disfagia: G3: 10% G4: 0% Haematological toxicity G3: 5% G4: 0 G5: 0%)
OR**: 86%	OR: 75%	OR: 92%	OR: 65%	OR: 85%
2-year LC***: 64.2% 2-year OS****:64.6%	2-year LC: 57.8% 2-year OS: 56.2%	2-year LC: 66.4% 2-year OS: 75.5%	2-year LC: 70.1% 2-year OS: 66.7%	2-year LC: 76.5% 2-year OS: 82.4%%

* IRMA : Intensified Radiotherapy by multimodality Association in H&N cancer
CF: Cisplatin + 5Fluoruracile ; C: Cisplatin (30 mg / m2) ; DCF: Docetaxel + Cisplatin + 5Fluoruracile; Cetuximab (400 mg / m2): ** OR: Overall response; ***LC: Local control; ****OS : Overall survival.

Conclusion: In our experience moderately hypofractionated and accelerated radio-chemotherapy after induction chemotherapy was feasible. Intensive patient monitoring and supportive strategies during chemoradiation are necessary to manage of side effects.

EP-1039

H&N IMRT: correlation of dysphagia/xerostomia to dose/volume parameters of involved OARs

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Purpose or Objective: To analyse the frequency and severity of dysphagia and xerostomia in patients affected by nasopharyngeal and oropharyngeal cancers treated by intensity-modulated radiotherapy (IMRT) and the correlation with volumetric variations and dosimetric data of pharyngeal constrictor muscles and parotid glands.

Material and Methods: Fifty patients, who underwent adaptive IMRT for nasopharyngeal and oropharyngeal cancers, were included in the present study. Eighty-four percent of patients (42/50) received concurrent radio-chemotherapy and 92% (44/50) were in locally advanced stage. Dose-volume parameters related to constrictor muscles (superior constrictor muscle, SCM; middle constrictor muscle, MCM; inferior constrictor muscle, ICM and whole pharyngeal constrictor muscle, CM), and parotid glands were analyzed using dose-volume histograms (DVHs). All patients underwent replanning CT scan after 5 weeks of radiation therapy and the target and OARs were re-contoured on fusion images after co-registration. The volumetric variations of pharyngeal constrictor muscles and parotid glands were measured. Volumetric variations and dose-volume parameters were associated to acute and late dysphagia and xerostomia according to RTOG score, quality of life questionnaires (PSS-H&N e QLQ-H&N35), and oesophageal transit .

Results: Volumetric variations and dose-volume parameters of pharyngeal constrictor muscles and parotid glands are reported in Table 1. Adaptive IMRT achieved a good sparing of parotid glands (mean dose 24.9 Gy) and constrictor muscles (mean dose 51.2 Gy). Acute dysphagia, was scored as grade 0-1 in 18/50 patients (36%) and as grade 2-3 in 32/50 (64%). Acute xerostomia, was scored as grade 0-1 in 21/50 patients (42%) and as grade 2-3 in 29/50 (58%). Volumetric variations and dose-volume parameters of the constrictor muscles and parotid glands did not correlate with acute toxicity ($p>0.05$). At 2 years median follow-up (range 6-67 months), late dysphagia was scored as grade 0-1 in 40/50 of patients (80%) and as grade 2-3 in 10/50 (20%). Late xerostomia was scored as grade 0-1 in 42/50 of patients (84%) and as grade 2-3 in 8/50 (16%). The analysis of the correlation of volumetric variations and dose-volume parameters with clinical data (RTOG score for late toxicity, quality of life questionnaires and oesophageal transit) is ongoing.

OAR	Median Volume (cc)	Replanning median Volume (cc)	Δ volume (%)	Median maximum dose (Gy)	Median mean dose (Gy)
SCM	6.9	8.5	+20	71.9	62.7
MCM	2.1	2.6	+17	65.2	51.5
ICM	3.1	3.7	+11	60.1	42.9
CM	12.0	14.7	+17	71.9	51.2
Right parotid gland	25.0	17.8	-24		24.9
Left parotid gland	22.6	16.2	-32		24.9

Conclusion: During radiotherapy, pharyngeal constrictor muscles and salivary glands underwent volumetric variations. Volumetric variations and dosimetric findings did not correlate with acute toxicity, probably because of the complexity and multifactorial pathogenesis of acute dysphagia and xerostomia. The ongoing analysis on the correlation of late toxicity data with volumetric variations and dose-volume parameters may help in the optimization of IMRT treatment planning.

EP-1040

Development of a CT-based prognostic model for regional control in head and neck cancer after RT

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Purpose or Objective: At our center, the need for neck dissection (ND) after radiotherapy (RT) is determined based on the nodal response on the post-RT Computed Tomography (CT) study 4 months after the end of treatment. We want to report the outcome of this approach and investigate whether characteristics on pre- and post- RT CT studies can predict the necessity of post-RT ND.

Material and Methods: Between 2002 and 2012, 183 consecutive patients with lymph node-positive head and neck cancer (HNC) were treated with RT or concurrent chemoradiotherapy (CRT) without planned ND. CT studies pre- and post-treatment were reviewed for lymph node size and presence of necrosis, extracapsular spread and calcifications. At patient level, data were correlated with 3 year regional control (RC), metastasis free survival (MFS), disease free survival (DFS) and overall survival (OS). At nodal level, data were correlated with relapse of the individual lymph nodes (LNR). A stepwise selection procedure was followed to construct a multivariable prediction model for regional relapse (RR) within 3 years. The area under the ROC curve (AUC) was determined for the selected model. Additionally a bootstrap-corrected AUC value was calculated. This AUC value corrects for overoptimism resulting from the fact that model construction and model validation were performed on the same data set.

Results: The median follow-up was 60 months. 3-year outcome rates were as follows: LC of 84%, RC of 80%, MFS of 74%, DFS of 61%, OS of 63%. Pre-treatment nodal size at patient- and nodal level and presence of necrosis at patient level were associated with a poorer outcome. This was also the case for post-treatment lymph node size and presence of necrosis and extracapsular spread (Table 1). Based on our results we developed a multivariate model for RR prediction. After performing a stepwise selection procedure pre-RT T stage (p=0.02), post-RT necrosis (p=0.03) and post-RT largest nodal diameter (p=0.01) were included in the model. The AUC of this model was 0.78 (95% CI 0.63;0.84); the bootstrap-corrected AUC was 0.74 (95% CI 0.67; 0.89). The risk for RR within 3 years can be calculated using the following formula:

$$RR\,(\%) = \frac{e^{\mu}}{1 + e^{\mu}}$$

$$\mu = 0.085 * largest\ axial\ diameter\ (mm) + 0.6749 * (T\ stage) - 4.8482 + (only\ when\ necrosis)\ 1.1384$$

Table 1: Predictive value of post-treatment CT characteristics for outcome

CT characteristic	Outcome	OR/HR (95% CI)	p-value
∑ nodal volume			
	RR	OR 1.262 (1.072;1.486)	0.0051
	MFS	nonlinear trend	
	DFS	HR 1.051 (1.028;1.074)	<0.0001
	OS	HR 1.056 (1.035;1.078)	<0.0001
∑ nodal volume 2cm³ vs 1cm³	MFS	HR 1.152 (1.054;1.259)	0.0018
Largest diameter			
	RR	OR 1.108 (1.047;1.172)	0,0004
	MFS	HR 1.043 (1.014;1.072)	0.0036
	DFS	HR 1.059 (1.035;1.083)	<0.0001
	OS	nonlinear trend	<0.0001
Largest diameter > 31.8 mm	OS	HR 5.764 (2.851;11.651)	<0.0001
Necrosis			
	RR	OR 5.960 (2.410;14.738)	0.0001
	MFS	HR 2.203 (1.186;4.092)	0.0124
	DFS	HR 2.668 (1.671;4.262)	<0.0001
	OS	HR 2.406 (1.529;3.785)	0.0001
Calcifications			
	RR	OR 0.643 (0.167;2.483)	0.5189
	MFS	HR 0.950 (0.373;2.421)	0.9143
	DFS	HR 0.843 (0.404;1.759)	0.6494
	OS	HR 0.863 (0.430;1.729)	0.6772
ECS			
	RR	OR 3.451 (1.056;11.283)	0.0404
	MFS	HR 2.482 (1.144;5.385)	0.0214
	DFS	HR 2.343 (1.275;4.303)	0.0061
	OS	HR 1.800 (0.971;3.337)	0.0620

Abbreviations: CT = computed tomography; OR = odds ratio; HR = hazard ratio; CI = confidence interval; ∑ = sum; RR = regional recurrence; MFS = metastasis-free survival; DFS = disease-free survival; OS = overall survival; ECS = extracapsular spread.

Conclusion: Characteristics on the post-RT CT study can predict the likelihood of residual lymph node disease and outcome. Characteristics on the pre-therapy CT study seem less useful for this purpose. A CT-based multivariate prognostic model based on our findings was developed which can aid in predicting RR.

EP-1041

Evaluation of dysphagia in head and neck cancer patients undergoing Intensity Modulated Radiotherapy

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Purpose or Objective: With the success of Intensity Modulated Radiotherapy (IMRT) techniques in reducing the severity of xerostomia in head and neck cancer (HNC) patients, efforts should be made to improve swallowing dysfunction, which is potentially even more discomforting and incapacitating side effect and adversely affects the quality of life. This is a clinical dosimetric study to investigate the correlation between radiation doses delivered to organs at risk for radiation induced swallowing dysfunction (SWOARs) and severity of dysphagia following concurrent chemoradiotherapy to HNC patients and evaluate various factors which assume importance in determining the risk of dysphagia/aspiration.

Material and Methods: 60 Head and Neck cancer patients (Oropharynx 28, Hypopharynx 12 and Larynx 20) were enrolled between May 2013 and June 2014 for this prospective longitudinal study after prior approval from the hospital ethics and review committee. Patients were treated with curative intent by radiotherapy using IMRT and concurrent chemotherapy using cisplatin (40 mg/m2) on weekly basis. Delineation of SWOARs was done using RTOG guidelines and following structures were contoured: superior, middle and inferior pharyngeal constrictor, cricopharyngeal muscle, esophageal inlet muscle, cervical esophagus, base of tongue, supraglottic and glottic larynx. Dysphagia endpoints included both patient-reported (EORTC Head and Neck Quality of Life instrument and MD Anderson Dysphagia Inventory) and observer-rated scores (Common Terminology Criteria for Adverse Events- CTCAE v4.0 and RTOG/EORTC Late Radiation Morbidity Scoring). Patients were assessed weekly during radiation and at 1 month and 3 months after completion of treatment. Correlation between dysphagia and radiation doses to SWOARs was assessed.

Results: With an increase in the mean dose to the SWOARs, the grades of dysphagia also increased. After 3 months of completion of treatment, 27% patients had persistent dysphagia of grade 3 or grade 4. Significant correlation was observed between patient reported dysphagia scores and the mean doses to the superior and middle pharyngeal constrictor as well as glottic and supraglottic larynx ($p<0.05$). Observer rated dysphagia scores correlated significantly with mean superior pharyngeal constrictor dose and not with dose to other SWOARs. Two patients of carcinoma hypopharynx developed stricture which correlated significantly with dose to esophageal inlet muscle.

Conclusion: Radiotherapy plans sparing SWOARs should be generated and implemented to prevent the problem of dysphagia. The structures whose damage may cause dysphagia and aspiration are the pharyngeal constrictors and the glottic and supraglottic larynx. Further studies are required to evaluate dose constraints to these SWOARs to reduce the incidence of radiation induced dysphagia and thus further improve the quality of life in HNC patients.

EP-1042

Risk-factors in pT1-2N0M0 squamous cancers of the oral cavity and the role of adjuvant radiotherapy

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